

CLAIMS

1. An isolated protein, called ASAP, characterized in that it is selected from the group consisting of:

5 a) a protein corresponding to the sequence represented in the attached sequence listing under the number SEQ ID NO: 1, corresponding to the human ASAP protein, and

10 b) a protein exhibiting, over its entire sequence, at least 80% identity or at least 90% similarity, preferably at least 90% identity or at least 95% similarity, with the protein of sequence SEQ ID No: 1.

2. The protein as claimed in claim 1, characterized in that it has the sequence SEQ ID NO: 46 corresponding to the murine ASAP protein.

3. A peptide, characterized in that it consists of a fragment of at least 10 consecutive amino acids of a protein as claimed in claim 1 or claim 2.

4. The peptide as claimed in claim 3, characterized in that it is selected from the sequences represented in the attached sequence listing under the numbers SEQ ID NO: 2 to SEQ ID NO: 14 and SEQ ID NOs: 47 to 53.

5. A protein that is a variant of the sequence SEQ ID NO: 1 or of the sequence SEQ ID NO: 46, characterized in that it has a mutation that results in a dysfunction of the protein.

6. The protein or peptide as claimed in any one of claims 1, 3, 4 or 5, characterized in that it is a protein or a peptide of human origin.

7. An isolated polynucleotide corresponding to a sequence selected from the group consisting of:

- the sequences encoding a protein or a peptide

as claimed in any one of claims 1 to 6;

- the sequences represented under the numbers SEQ ID NO: 15 and SEQ ID NO: 45 in the attached sequence listing, corresponding respectively to the human and murine ASAP cDNAs;

- the genomic DNA fragment of 29800 nucleotides corresponding to the sequence represented in the attached sequence listing under the number SEQ ID NO: 16, corresponding to the human *asap* gene;

- a fragment of at least 15 consecutive nucleotides of any one of the above sequences, with the exclusion of the sequences listed under the accession numbers AK024730 and AK024812 and of the ESTs listed under the accession numbers BU198882, BM693711,

AW372449, BM021380, BU928828, AL707573, AI885274, AI671785, AA805679, BU619959, BM021126, AL598336, AW976973, BU629726, AI433877, AV751613, BQ372751, AI827535, AI866257, AA843565, R96130, BU684090, BF958121, BQ351941, AW194906, BG203580, BF078132, AW486134, AL600279, AA025538, AL600264, BF170676, BU759494, BB025236, BF214179, AI283076, BE694273, AI266380, BM670854, AA968415, BU503982, BB700612, BE988355, BU058357, BB312934, AW061311, BM537962, BE988356, BB318982, BB311217, BB557152, BB185248, BB557128, BB698742, BB186736, AV345769, BB274293, BB632007, BB617958, AI391312, W18534, BB186581, BB311289, BB312835, AW347411, AA972439, BB263570, AU035125, BB277226, BB274224, BB268445, AW024037, AA025609, BB274174, R96089, BB272238, BB269037, BB385718, BE007324, BB325992, AJ275277, AI414381, BB125476, BB430961, BE232162, BQ121419, BQ121418, BG591509, BF457670, AL897593, AL897592, BM926692, BM538559, BI759567, AL601021, AL598780, AU222540, BG567619, AU166296, BF889835, AU164011, AV656025, BF343454, AW262441, AW237952 in the GenBank database;

- a fragment of any one of the above sequences, selected from the sequences represented in the attached

sequence listing under the numbers SEQ ID NO: 16 to SEQ ID NO: 30;

- a sequence exhibiting a percentage identity of at least 80%, preferably 90%, after optimal alignment, with one of the sequences or one of the fragments above;

- the sequences complementary to the above sequences, that may be sense or antisense.

8. The polynucleotide or fragment as claimed in claim 7, characterized in that it is a polynucleotide that is a variant of the sequence SEQ ID NO: 15 or 45.

9. The polynucleotide or fragment as claimed in claim 8, characterized in that it is a polynucleotide carrying at least one mutation that results in a modification of the amino acid sequence of the protein corresponding to the sequence SEQ ID NO: 1 or SEQ ID NO: 46.

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10. The use of a polynucleotide or of a fragment as claimed in any one of claims 7 to 9 or of one of the sequences listed under the accession numbers AK024730 and AK024812 and of one of the ESTs listed under the accession numbers BU198882, BM693711,

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AW372449, BM021380, BU928828, AL707573, AI885274, AI671785, AA805679, BU619959, BM021126, AL598336, AW976973, BU629726, AI433877, AV751613, BQ372751, AI827535, AI866257, AA843565, R96130,

BU684090, BF958121, BQ351941, AW194906, BG203580, BF078132, AW486134, AL600279, AA025538, AL600264, BF170676, BU759494, BB025236, BF214179, AI283076, BE694273, AI266380, BM670854, AA968415, BU503982, BB700612, BE988355, BU058357, BB312934, AW061311, BM537962, BE988356, BB318982, BB311217, BB557152, BB185248, BB557128, BB698742, BB186736, AV345769, BB274293, BB632007, BB617958, AI391312, W18534, BB186581, BB311289, BB312835, AW347411, AA972439, BB263570, AU035125, BB277226, BB274224, BB268445, AW024037, AA025609, BB274174, R96089, BB272238, BB269037, BB385718, BE007324, BB325992, AJ275277, AI414381, BB125476, BB430961, BE232162, BQ121419, BQ121418, BG591509, BF457670, AL897593, AL897592, BM926692, BM538559, BI759567, AL601021, AL598780, AU222540, BG567619, AU166296,

BF889835, AU164011, AV656025, BF343454, AW262441, AW237952 in the GenBank database, or of their fragments, as a probe for detecting, identifying or assaying polynucleotides
5 corresponding to the polynucleotide as claimed in any one of claims 7 to 9, particularly in other organisms.

11. The use as claimed in claim 10, characterized in that the probe is selected from the group consisting of
10 the sequences SEQ ID NO: 15, 45 or SEQ ID NO: 17 to SEQ ID NO: 44.

12. A primer for amplifying the polynucleotides (RNA or genomic DNA) corresponding to the polynucleotide as
15 claimed in any one of claims 7 to 9, particularly in other organisms, characterized in that it is selected from the group consisting of the sequences SEQ ID NO: 31 to 43.

20 13. A polynucleotide that can be obtained by amplification using the primers as claimed in claim 12.

14. A method for determining the transcription profile

of the gene corresponding to the polynucleotide as claimed in any one of claims 7 to 9 or 13, or an alteration in said profile, in a biological sample, comprising a first step consisting in obtaining, by any appropriate means, the total RNA from the biological sample, a second step consisting in bringing said RNA into contact with a probe as defined in claim 10 or 11, labeled beforehand, under conventional conditions for hybridization between the RNAs and the probe, and a third step consisting in revealing, by any appropriate means, the hybrids formed.

15. The method as claimed in claim 14, in which the second step is a step consisting of reverse transcription and/or amplification of the transcripts, carried out using a pair of primers as claimed in claim 12, and the third step is a step consisting in revealing, by any appropriate means, the amplified nucleic acids.

16. The method as claimed in either one of claims 14 and 15, characterized in that it also comprises a step consisting in evaluating the level of transcription of the gene by comparison with a control selected beforehand.

17. A method for demonstrating, in other species, the gene corresponding to the polynucleotide as claimed in any one of claims 7 to 9 or 13, or for demonstrating the allelic variants of said gene or demonstrating a functional alteration of this gene, in a biological sample, comprising a first step consisting in obtaining, by any appropriate means, the DNA from the biological sample, a second step consisting in bringing said DNA into contact with a probe as defined in claim 10 or 11, labeled beforehand, under conventional conditions for hybridization between the DNAs and the

probe, and a third step consisting in revealing, by any appropriate means, the hybrids formed.

18. The method as claimed in claim 17, in which the
5 second step is an amplification step carried out using primers as claimed in claim 12, and the third step is a step consisting in revealing, by any appropriate means, the amplified nucleic acids formed.

10 19. The method as claimed in either one of claims 17 and 18, characterized in that it also comprises a step consisting in isolating and sequencing the nucleic acids demonstrated.

15 20. A kit of reagents for carrying out the methods as claimed in any one of claims 14 to 19, comprising:

- at least one probe as defined in claim 10 or 11 and/or primers as claimed in claim 12;

- the reagents required for carrying out a
20 conventional hybridization reaction between said probe and/or said primers and the nucleic acid of the biological sample;

- the reagents required for carrying out an amplification reaction;

- 25 - the reagents required for detecting and/or assaying the hybrid formed between said probe and the nucleic acid of the biological sample or the amplified nucleic acids formed.

30 21. A cloning and/or expression vector into which a polynucleotide or a fragment as claimed in any one of claims 7 to 9 or 13 is inserted.

35 22. A transformed host cell into which at least one polynucleotide or one fragment as claimed in any one of claims 7 to 9 or 13 or at least one vector as claimed in claim 21 has been introduced.

23. A nonhuman transgenic organism in which all or some of the cells contain at least one polynucleotide or one fragment as claimed in any one of claims 7 to 9
5 or 123 or at least one vector as claimed in claim 20, in a free or integrated form.

24. The nonhuman transgenic organism as claimed in claim 23, characterized in that it carries cells
10 containing a polynucleotide as claimed in any one of claims 7 to 9 or 13, that is nonfunctional or carrying a mutation.

25. The use of a transformed cell as claimed in claim 22 or of a nonhuman transgenic organism as
15 claimed in either one of claims 23 and 24, for producing a protein or a peptide as claimed in any one of claims 1 to 6.

20 26. A method for preparing a protein or a peptide as claimed in any one of claims 1 to 6, characterized in that cells expressing the protein or transformed cells as claimed in claim 22 or a transgenic organism as claimed in either one of claims 23 and 24 cultured
25 under conditions that allow the expression of said protein, and in that said protein is purified.

27. A protein, characterized in that it can be obtained by means of the method of preparation as
30 claimed in claim 26.

28. A monoclonal or polyclonal antibody, characterized in that it is capable of specifically recognizing a protein or a peptide as claimed in any one of claims 1
35 to 6 or 27.

29. The antibody as claimed in claim 28, characterized

in that it recognizes, among MAPs, only and specifically the ASAP protein of sequence SEQ ID NO: 1 or SEQ ID NO: 46.

5 30. The use of an antibody as claimed in either one of claims 28 and 29, for detecting and/or purifying a protein as claimed in any one of claims 1 to 6 or 27.

10 31. A method for detecting a protein as claimed in any one of claims 1 to 6 or 27, in the cells of a biological sample, comprising

- a first step consisting in suitably treating the cells by any appropriate means for making the intracellular medium accessible,

15 - a second step consisting in bringing said intracellular medium thus obtained into contact with an antibody as claimed in either one of claims 28 and 29, and

20 - a third step consisting in demonstrating, by any appropriate means, the ASAP protein-antibody complex formed.

25 32. The use of an antibody as claimed in either one of claims 28 and 29, for detecting and/or selecting cells exhibiting disturbances in mitotic spindle organization and/or an induction of aberrant and abortive mitoses associated with overexpression of the protein as claimed in any one of claims 1 to 6 or 27.

30 33. A method for evaluating, *in vitro*, the proliferative capacity or aggressiveness of cancer cells, comprising

35 - a first step consisting in suitably treating the cells by any appropriate means for making the intracellular medium accessible,

- a second step consisting in bringing said intracellular medium thus obtained into contact with an

antibody as claimed in either one of claims 28 and 29,

- a third step consisting in demonstrating and measuring, by any appropriate means, the ASAP protein-antibody complex formed, and

5 - a fourth step consisting in evaluating the level of transcription of the gene by comparison of the level of ASAP protein-antibody complexes formed with that of a control biological sample selected beforehand.

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34. A kit for carrying out the method as claimed in either one of claims 31 and 33, comprising:

- at least one monoclonal or polyclonal antibody as claimed in either one of claims 28 and 29;

15 - the reagents for detecting the ASAP protein-antibody complex produced during the immunological reaction.

35. A method for screening for a substance capable of interacting, *in vitro*, directly or indirectly with the polynucleotide as claimed in any one of claims 7 to 9 or 13 or the protein or a peptide as claimed in any one of claims 1 to 6 or 27, characterized in that:

20 - in a first step, the substance to be tested is brought into contact with the polynucleotide or the protein, and

25 - in a second step, the complex formed between said substance and the polynucleotide or the protein is detected by any appropriate means.

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36. A method of screening for a substance capable of modulating the activity of the protein as claimed in any one of claims 1 to 6 or 27, characterized in that:

35 - in a first step, cells of a biological sample expressing the protein as claimed in any one of claims 1 to 6 or 27 are brought into contact with a substance to be tested,

- in a second step, the effect of said substance on the activity of said protein is measured by any appropriate means, and

- in a third step, substances capable of
5 modulating said activity are selected.

37. The protein as claimed in any one of claims 1 to 6 or 27, or a polynucleotide or fragment as claimed in any one of claims 7 to 9 or 13, or an antibody as
10 claimed in either one of claims 28 and 29, or a vector as claimed in claim 21, or a transformed cell as claimed in claim 22, used as medicinal products..

38. The use of a protein as claimed in any one of
15 claims 1 to 6 or 27, or of a polynucleotide or of a fragment as claimed in any one of claims 7 to 9 or 13, or of an antibody as claimed in either one of claims 28 and 29, or of a vector as claimed in claim 21, or of a transformed cell as claimed in claim 22, in the
20 preparation of an anti-mitotic medicinal product.

39. The use of an antisense polynucleotide or fragment as claimed in any one of claims 7 to 9 or 13, or of an antibody as claimed in either one of claims 28 and 29,
25 or of a vector containing an antisense oligonucleotide as claimed in claim 21, and capable of inhibiting the expression of the polynucleotide as claimed in any one of claims 7 to 9 or of the protein as claimed in any one of claims 1, 2, 5 or 6, in the preparation of a
30 medicinal product intended for the treatment of pathologies associated with disturbances in mitotic spindle organization and/or with an induction of aberrant and abortive mitoses, associated with overexpression of the protein as claimed in any one of
35 claims 1 to 6 or 27.